

In the Claims:

Please add new claims 145-149 as follows.

Please cancel, without prejudice, claims 1-72, 99, 101-102, 104-105, 110-113, 116, 118-119 and 122-123.

Please amend claims 98, 106-109, 114-115, 120, 124-127 and 142-143 as follows:

1-72.(Canceled)

73.(Withdrawn) An isolated nucleic acid sequence encoding a human lysosomal protein being contiguously linked to a C-terminal vacuolar targeting signal and an N-terminal endoplasmic reticulum signal peptide.

74.(Withdrawn) An isolated nucleic acid sequence encoding a human lysosomal protein being contiguously linked to a C-terminal endoplasmic reticulum retention signal and an N-terminal endoplasmic reticulum signal peptide.

75.(Withdrawn) The isolated nucleic acid sequence of claim 73, wherein wherein said human lysosomal protein is a glucocerebrosidase.

76.(Withdrawn) The isolated nucleic acid sequence of claim 73, wherein said human lysosomal protein is a human α -galactosidase.

77.(Withdrawn) The isolated nucleic acid sequence of claim 74, wherein said human lysosomal protein is a human glucocerebrosidase.

78.(Withdrawn) The isolated nucleic acid sequence of claim 74, wherein said human lysosomal protein is a human α -galactosidase.

79.(Withdrawn) The isolated nucleic acid of claim 73, wherein said vacuolar targeting signal is a basic tobacco chitinase A gene vacuolar targeting signal.

80.(Withdrawn) The isolated nucleic acid of claim 79, wherein said vacuolar targeting signal is as set forth in SEQ ID NO: 2.

81.(Withdrawn) The isolated nucleic acid of claim 73, wherein said endoplasmic reticulum signal peptide is as set forth in SEQ ID NO: 1.

82.(Withdrawn) The isolated nucleic acid of claim 73, wherein said human lysosomal protein comprises an amino acid sequence as set forth in SEQ ID NO: 8.

83.(Withdrawn) The isolated nucleic acid of claim 73, wherein said nucleic acid sequence is as set forth in SEQ ID NO: 7.

84.(Withdrawn) The isolated nucleic acid of claim 73, wherein said nucleic acid sequence is as set forth in SEQ ID NO: 13.

85.(Withdrawn) The isolated nucleic acid of claim 73, further comprising a promoter functional in plant cells transcriptionally linked to said nucleic acid sequence.

86.(Withdrawn) The isolated nucleic acid of claim 85, wherein said promoter sequence is a Cauliflower Mosaic Virus S-35 promoter sequence.

87.(Withdrawn) The isolated nucleic acid of claim 73, further comprising a transcriptionally linked terminator sequence functional in plant cells.

88.(Withdrawn) The isolated nucleic acid of claim 73, wherein said isolated nucleic acid sequence optionally further comprises additional operably linked control, promoting and regulatory elements and/or selectable markers.

89.(Withdrawn) The isolated nucleic acid of claim 88, wherein said terminator is an octopine synthase terminator of *Agrobacterium tumefaciens*, and the regulatory element is the TMV (Tobacco Mosaic Virus) omega translational enhancer element.

90.(Withdrawn) A nucleic acid construct capable of expression in a plant cell comprising the isolated nucleic acid of claim 73.

91.(Withdrawn) A cell comprising the nucleic acid construct of claim 90.

92.(Withdrawn) The cell of claim 91, recombinantly producing said human lysosomal enzyme.

93.(Withdrawn) The cell of claim 92, wherein said human lysosomal protein is recombinantly produced so as to have at least one xylose and at least one exposed mannose residue.

94.(Withdrawn) The cell of claim 91, wherein said cell is a plant cell.

95.(Withdrawn) The cell of claim 94, wherein said plant cell is a plant root cell selected from the group consisting of *Agrobacterium rhizogenes* transformed root cell, celery cell, ginger cell, horseradish cell and carrot cell.

96.(Withdrawn) The cell of claim 95, wherein said plant cell is a carrot cell.

97.(Withdrawn) The cell of claim 91, wherein said cell is an *Agrobacterium tumefaciens* cell.

98.(Currently amended) A human lysosomal protein comprising at least one xylose residue and at least one exposed mannose residue, wherein said human lysosomal protein comprises an amino acid sequence encoded by the nucleic acid as set forth in SEQ ID NO: 7 and wherein said human lysosomal protein is contiguously linked at its C terminus to a vacuolar targeting signal peptide and at its N-terminus to an N-terminal endoplasmic reticulum signal peptide.

99.(Canceled)

100.(Previously presented) The human lysosomal protein of claim 98, further comprising at least one fucose residue having an alpha (1-3) glycosidic bond.

101.(Canceled)

102.(Canceled)

103.(Withdrawn) The human lysosomal protein of claim 98, wherein said lysosomal enzyme is an α -galactosidase.

104.(Canceled)

105. (Canceled)

106.(Currently amended) The human lysosomal protein of claim ~~98~~105, wherein said vacuolar targeting signal peptide is a basic tobacco chitinase A gene vacuolar targeting signal.

107. (Currently amended) The human lysosomal protein of claim 106, wherein said vacuolar targeting signal peptide comprises ~~is as set forth in~~ SEQ ID NO: 2.

108.(Currently amended) The human lysosomal protein of claim ~~98~~105, wherein said endoplasmic reticulum signal peptide comprises ~~is as set forth in~~ SEQ ID NO: 1.

109.(Currently amended) The human lysosomal protein of claim ~~98~~102, wherein said amino acid sequence ~~human glucocerebrosidase comprises~~ the amino acid sequence as set forth in SEQ ID NO: 8.

110-113. (Canceled)

114.(Currently amended) A pharmaceutical composition comprising the human lysosomal protein of claim 989 and a pharmaceutically acceptable carrier.

115.(Currently amended) A plant cell preparation comprising a human lysosomal protein comprising at least one xylose residue and at least one exposed mannose residue wherein said human lysosomal protein comprises an amino acid sequence encoded by the nucleic acid as set forth in SEQ ID NO: 7 and wherein said human lysosomal protein is contiguously linked at its C terminus to a vacuolar targeting signal peptide and at its N-terminus to an N-terminal endoplasmic reticulum signal peptide.

116. (Canceled)

117.(Previously presented) The plant cell preparation of claim 115, further comprising at least one fucose residue having an alpha (1-3) glycosidic bond.

118. (Canceled)

119. (Canceled)

120.(Currently amended) The plant cell preparation of claim 115, wherein said human lysosomal protein comprises ~~thean~~ amino acid sequence as set forth in SEQ ID NO: 8.

121.(Withdrawn) The plant cell preparation of claim 115, wherein said lysosomal protein is a human α -galactosidase.

122. (Canceled)

123. (Canceled)

124.(Currently amended) The plant cell preparation of claim ~~115~~122, wherein said vacuolar targeting signal peptide is a basic tobacco chitinase A gene vacuolar targeting signal.

125.(Currently amended) The plant cell preparation of claim ~~124~~, wherein said vacuolar targeting signal peptide comprises~~is as set forth in~~ SEQ ID NO: 2.

126.(Currently amended) The plant cell preparation of claim ~~115~~23, wherein said endoplasmic reticulum signal peptide comprises~~is as set forth in~~ SEQ ID NO: 1.

127.(Currently amended) The plant cell preparation of claim 115, wherein said human lysosomal protein having at least one xylose residue and at least one exposed mannose residue is the main glycan structure~~comprises a dominant fraction of the lysosomal proteins of said plant cell preparationsaid lysosomal protein~~, as measured by linkage analysis.

128.(Previously presented) A pharmaceutical composition comprising the plant cell preparation of claim 115 and a pharmaceutically acceptable carrier.

129.(Withdrawn) A method of producing a lysosomal protein comprising:
preparing a culture of recombinant cells transformed or transfected with the nucleic acid construct of claim 90; and
culturing said cell culture under conditions permitting the expression of said protein, wherein said protein produced by said cells comprises at least one xylose residue.

130.(Withdrawn) The method of claim 129, wherein said cell culture is cultured in suspension.

131.(Withdrawn) The method of claim 129, further comprising:
purifying said protein.

132.(Withdrawn) The method according to claim 129, wherein said protein produced by said cell has at least one xylose and at least one exposed mannose residue.

133.(Withdrawn) The method according to claim 131, wherein said lysosomal protein binds to a mannose receptor on a macrophage.

134.(Withdrawn) The method according to claim 129, wherein said lysosomal protein has increased affinity for said macrophage, in comparison with the corresponding affinity of a naturally occurring lysosomal protein to said macrophage.

135.(Withdrawn) Use of a biologically active lysosomal enzyme as defined by claim 110, in the manufacture of a medicament for the treatment or prevention of a lysosomal storage disease.

136.(Withdrawn) The use of claim 135, wherein said lysosomal enzyme has increased affinity for macrophage cells, in comparison with the corresponding affinity of a naturally occurring lysosomal enzyme to said macrophage cells.

137.(Withdrawn) The use according to claim 135, wherein said disease is Gaucher's disease.

138.(Withdrawn) A method for treating a subject having lysosomal storage disease using a biologically active recombinant lysosomal enzyme, comprising:

- (a) providing a recombinant biologically active lysosomal enzyme as defined in claim 110; and
- (b) administering a therapeutically effective amount of said recombinant biologically active lysosomal enzyme to said subject.

139. (Withdrawn) The method according to claim 138, wherein said lysosomal enzyme is glucocerebrosidase (GCD).

140. (Withdrawn) The method according to claim 138, wherein said lysosomal storage disease is Gaucher's disease.

141. (Withdrawn) The method according to claim 138, wherein said target cell at the target site is a Kupffer cell in the liver of said subject.

142. (Currently amended) A human lysosomal protein comprising a human glucocerebrosidase which comprises ~~the~~^a amino acid sequence as set forth in SEQ ID NO: 8, wherein said human glucocerebrosidase is ~~contiguously~~ linked at its C-terminus to ~~the~~^a C-terminal-vacuolar targeting signal peptide as set forth in SEQ ID NO: 2 and at its ~~an~~^a N-terminus to ~~the~~^a endoplasmic reticulum signal peptide as set forth in SEQ ID NO: 1.

143. (Currently amended) A ~~The~~ human lysosomal protein comprising a human glucocerebrosidase of claim 142, which ~~which~~ comprises ~~the~~^a amino acid sequence as set forth in SEQ ID NO: 14.

144. (Previously presented) A pharmaceutical composition comprising the human lysosomal protein of claim 142 and a pharmaceutically acceptable carrier.

145. (New) A pharmaceutical composition comprising the human lysosomal protein of claim 143 and a pharmaceutically acceptable carrier.

146. (New) A human lysosomal protein comprising a human glucocerebrosidase which comprises the amino acid sequence encoded by the polynucleotide as set forth in SEQ ID NO: 7, wherein said human glucocerebrosidase comprises at least one xylose residue and at least one exposed mannose residue, and is linked at its C-terminus to a vacuolar targeting signal peptide.

147. (New) The human lysosomal protein of claim 146, having a glucocerebrosidase hydrolase activity.

148. (New) The human lysosomal protein of claim 147, having uptake into macrophages.

149. (New) A human lysosomal protein comprising a human glucocerebrosidase which comprises the amino acid sequence encoded by the polynucleotide as set forth in SEQ ID NO: 7, wherein said human glucocerebrosidase is linked at its C-terminus to a vacuolar targeting signal peptide.